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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/596,675	06/21/2006	Bandi Parthasaradhi Reddy	H1089/20035	9298

3000 7590 10/07/2009  
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PHILADELPHIA, PA 19103-2212

EXAMINER
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SACKEY, EBENEZER O

ART UNIT	PAPER NUMBER
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1624

NOTIFICATION DATE	DELIVERY MODE
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10/07/2009

ELECTRONIC

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patents@crbcp.com

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	10/596,675	PARTHASARADHI REDDY ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	EBENEZER SACKEY	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 21 June 2006.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1-58 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 22-24 and 37-58 is/are allowed.
- 6) ☒ Claim(s) 1-21 and 25-36 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)            | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. _____                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>06/21/06</u> .  | 6) <input type="checkbox"/> Other: _____                          |

## **DETAILED ACTION**

### **Status of the Claims**

Claims 1-58 are pending.

### ***Specification***

The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

### ***Information Disclosure Statement***

Receipt of the Information Disclosure Statement filed on 06/21/06 is acknowledged and has been entered into the file. A signed copy of the 1449 is attached herewith.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

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The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicants claim the conversion of compound(s) of formula (I) to its solvated form. However, it is not clear how the conversion is achieved from the compound to the solvated form. Additionally, formula (I) is not disclosed in claim 1, thus rendering the claim and claims depended therefrom indefinite.

### **Claim Rejections - 35 U.S.C. § 103**

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

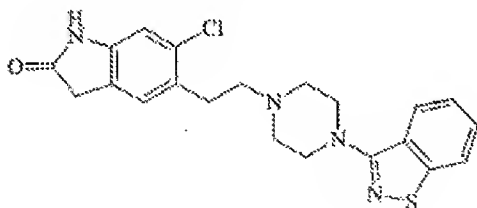
2. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.

2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

3. Claims 1-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lowe et al., U.S. Patent Number 4,831,031 in view of Howard et al., "Synthesis of  $^3\text{H}$ - and  $^{14}\text{C}$ -Labelled CP-88,059:" A POTENT ATYPICAL ANTIPSYCHOTIC AGENT; Journal of Labelled Compounds and Radiopharmaceuticals; Vol. XXXIV, No. 2; pages 117-125.

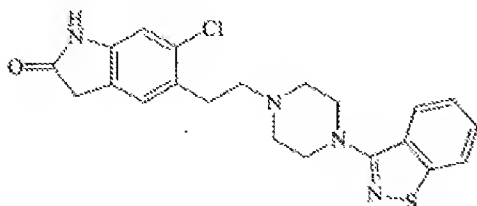
Applicants claim a process for preparing compounds of formula (I), comprising silylating 1-(1,2-benzisothiazol-3-yl)piperazine of formula (II) with a silylating agent to form compound of formula (III) and subsequently reacting formula (III) with compound of formula (iv) in a solvent in the presence of a base at  $40^{\circ}\text{C}$  to obtain formula (I) and optionally convert the compound to its solvate, acid addition salts and hydrate.



#### **Determination of the scope and content of the prior art (MPEP §2141.01)**

Lowe et al., teach a process for preparing compounds of formula (I) which comprises reacting compounds of non-silylated formula (II) with compounds of formula (IV). See the entire reference especially Example 16.

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**Ascertainment of the difference between the prior art and the claims (MPEP****§2141.02)**

The difference between the instant process and that of Lowe '031' is that, '031' is silent on the use of a specific silylated compound. However, from a reading of the specification, the silylated reactant (formula (III)) do not appear to provide any advantage to the current process and the compound produced in terms of bio-availability.

Additionally, Howard et al., teach that the use of an analogous silylated compound for the making of ziprasidone is known and expected to succeed. See the entire reference, especially Scheme 2.

Note the various forms and derivatives of ziprasidone and the various means of preparing same by the use of neutralizing agents such as sodium carbonate, column 2, lines 46-48' bases such as tertiary amines, column 2, lines 43-44, triethylsilane as taught by Howard et al., and refluxing of the reaction system as noted in column 2, line 56 of Lowe. Thus, the preparation of a known compound (in this instant ziprasidone) is considered *prima facie* obvious when all the necessary reactants are known.

Moreover, changing the form, purity or other characteristics of an old compound is considered *prima facie obvious* and does not render the novel form patentable where the difference in form, purity or characteristics is inherent in the prior art, *In re Best*, 562 F 2d. 1252, 1254, 195 U.S.P.Q 430, 433 (CCPA 1977). Also note that the use of any of the forms claimed herein will lead to the formation of ziprasidone and can thus, be considered *prima facie* obvious. Note solvents of claims 8, 9, 10, 13 and 14 and bases of claims 16 and 17 which are known and are *obvious* modifications well within the

purview of the skilled artisan. The variables are merely optimization of variables, which are not patentable absent unexpected result due to these variables since the prepared compound is structurally and chemically the same as claimed herein. Note *In re Boesch*, 205 U.S.P.Q. 215 (1980) and *In re Aller* 105 U.S.P.Q. 233 (1955).

**Finding of prima facie obviousness---rational and motivation (MPEP §2142-2143)**

Accordingly, at the time of filing this application, it would have been *prima facie* obvious to one of ordinary skill in the art to prepare ziprasidone and salts as disclosed by Lowe et al., with a reasonable expectation that the resulting product would be pure because Howard et al., discloses that ziprasidone can be prepared from an analogous silylated compound as disclosed by the reference (Scheme 2). Hence, one in possession of Lowe et al., and Howard et al., is in possession of the instant process absent a showing of unexpected results and/or properties. The process that is being claimed is a predictable and expected process.

**Claim Rejections - 35 U.S.C. § 103**

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

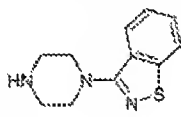
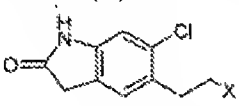
(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

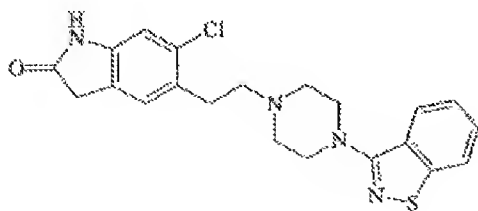
5. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

6. Claims 25-36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Busch et al., (WO 03/070246) and Lowe et al., U.S. Patent Number 4,831,031 each taken alone.

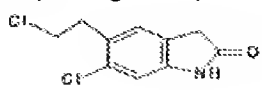
Applicants claim a process for preparing compounds of formula (I), comprising reacting

1-(1,2-benzisothiazol-3-yl)piperazine of formula (II)  with a 5-(2-haloethyl)-6-chloro-oxindole of formula IV  to obtain formula (I) and optionally convert the compound to its solvate, acid addition salts and hydrate.

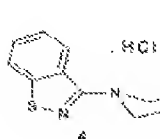


#### Determination of the scope and content of the prior art (MPEP §2141.01)

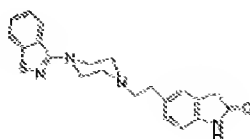
Busch et al., teach a process for preparing compounds of formula (I) which comprises

reacting compound of formula (3)  with compound of formula (4)

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to obtain formula (I)



. See the entire reference

especially pages 15 and 16, Schemes 1 and 2.

### Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

The difference between the instant process and that of Busch is that Busch teaches the preparation and isolation of various intermediate compounds. Additionally, note Lowe et al., teach that the use of various solvents such as amines (i.e., tertiary amines and carbonates) during the preparation of ziprasidone is known and, expected to succeed. See column 2, lines 40-49 and Example 16.

Thus, the preparation of a known compound (in this instant ziprasidone) is considered *prima facie* obvious when all the necessary reactants are known. Moreover, changing the form, purity or other characteristics of an old compound is considered *prima facie obvious* and does not render the novel form patentable where the difference in form, purity or characteristics is inherent in the prior art, *In re Best*, 562 F 2d. 1252, 1254, 195 U.S.P.Q 430, 433 (CCPA 1977). Also note that the use of any of the forms claimed herein will lead to the formation of ziprasidone and can thus, be considered *prima facie* obvious. Note solvents of claims 8, 9, 10, 13 and 14 and bases of claims 16 and 17 which are known and are *obvious* modifications well within the purview of the skilled artisan. The variables are merely optimization of variables, which are not patentable absent unexpected result due to these variables since the prepared compound is structurally and chemically the same as claimed herein. Note *In re Boesch*, 205 U.S.P.Q. 215 (1980) and *In re Aller* 105 U.S.P.Q. 233 (1955).

### Finding of *prima facie* obviousness---rational and motivation (MPEP §2142-2143)

Accordingly, at the time of filing this application, it would have been *prima facie* obvious to one of ordinary skill in the art to prepare ziprasidone and salts as disclosed by Busch et al., and Lowe et al., with a reasonable expectation that the resulting product would be pure because each of the references discloses that ziprasidone can be prepared from the required reactants (compounds). Hence, one in possession of Busch et al., and Lowe et al., is in possession of the instant process absent a showing of unexpected results and/or properties. The process that is being claimed is a predictable and expected process.

***Allowable Subject Matter***

The following is a statement of reasons for the indication of allowable subject matter: None of the prior art teaches a silylated compound as shown in claims 22-24 nor the process for preparing same (claims 37-58).

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to EBENEZER SACKKEY whose telephone number is (571)272-0704. The examiner can normally be reached on 7.30-4.30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

**/Ebenezer O. Sackey/  
Patent Examiner, AU 1624**

**/James O. Wilson/  
Supervisory Patent Examiner, AU 1624**